Adenoma of the Iris Pigment Epithelium: A Report of 20 Cases

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Background: Adenoma of the iris pigment epithelium (IPE) is an uncommon lesion that can simulate iris or ciliary body melanoma, melanocytoma, and pigment epithelial cyst.

Objectives: To evaluate the clinical and pathological features and prognosis of adenoma of the IPE in patients managed by us and to elucidate the features that help to differentiate this tumor from iris melanoma and other similar conditions.

Patients and Methods: The medical records of 20 patients with adenoma of the IPE were reviewed, and the clinical and histopathologic features were tabulated.

Results: Ten patients were male and 10 were female, with a mean age of 60.0 years (range, 11-85 years). All patients were referred because of suspected iris or ciliary body melanoma. All lesions were solitary and unilateral. Sixteen were located in the peripheral iris; 2, in the midzone; and 2, near the pupillary margin. Clinically, all tumors were abruptly elevated, all but 1 were dark gray to black, and all had a smooth, but sometimes multinodular, surface. The tumors caused thinning or complete effacement of the overlying iris stroma, but they did not directly involve the stroma. They typically blocked light with transillumination. On ultrasound biomicroscopy findings, adenoma of the IPE shows a solid tumor pattern, sometimes with small cystoid spaces. The tumor was managed by local resection in 2 patients and observation in 18, all of whom have been stable, with follow-up ranging from 6 months to 9 years. Histopathologic examination revealed a tumor originating in the IPE consisting of cords of pigment epithelial cells separated by septae of connective tissue.

Conclusions: Adenoma of the IPE usually has characteristic features that should differentiate it from iris melanoma, ciliary body melanoma, iris melanocytoma, and iris cyst. Adenoma of the IPE is a benign tumor that may remain relatively stable for years.


The IRIS pigment epithelium (IPE) can sometimes undergo reactive proliferation and migration, but true neoplasms of the IPE (adenoma and adenocarcinoma) are very uncommon.1,2 There have been only a few cases reported in the English-language literature during the last 50 years.3-18 In a recent review, Spraul et al18 cited a few additional cases from the world literature and rejected other reported cases because of poor documentation. Most available clinical information about these lesions is derived from case reports or very small series that were documented histopathologically after enucleation or local resection for suspected malignant melanoma.3,18 Hence, there is relatively little available information about the clinical variations and the clinical course of adenoma of the IPE.

We report herein our personal clinical experience with 20 patients in whom we diagnosed adenoma of the IPE. We present the clinical variations, ultrasonographic features, histopathologic findings, and clinical course of this tumor and describe the features that help differentiate it from iris melanoma, nevus, melanocytoma, and IPE cyst.

RESULTS

There were 20 patients with the diagnosis of adenoma of the IPE who first underwent evaluation by us from October 1, 1977, through April 30, 1997 (Table). The mean age at the time of referral to us was 60.0 years (range, 11-85 years; median, 59 years). There were 10 male and 10 female patients. Seventeen patients were white; 2 patients, African American; and 1 patient, Hispanic. The right eye was af-
PATIENTS AND METHODS

The medical records of all patients coded with the diagnosis of adenoma of the IPE were reviewed, and the clinical features, clinical course, and type of management were determined. General data collected included patient age, race, sex, referring diagnosis, previous management, history of ocular trauma or inflammation, associated ocular and systemic disease, ocular symptoms, and visual acuity.

Tumor data included tumor location (meridional), tumor size (basal diameter and thickness in millimeters) as measured using slitlamp examination and transillumination, surface features, color, and secondary effects on adjacent structures. The method of management was tabulated, and follow-up information was obtained. Histopathologic features in tumors excised surgically were assessed. Based on these observations, we make recommendations regarding the clinical diagnosis and management of adenoma of the IPE.

affected in 9 patients; the left eye, in 11. No patient had a history of ocular inflammation or trauma.

Visual acuity (herein stated in meters) in the affected eye ranged from 6/6 to finger counting (Table). In 17 patients, visual acuity was normal, ranging from 6/6 to 6/9. In 2 patients with mild to moderate visual loss in the affected eye (patients 9 and 19), the decreased vision was due to cataract and macular degeneration, respectively, neither of which appeared to be related to the iris tumor. In only 1 patient (patient 4) was minimal visual loss to 6/12 attributable to the tumor. In that case, the tumor had produced a slight subluxation of the lens.

All 20 tumors were unilateral and had distinct, abruptly elevated borders; 19 were dark gray to black in color (Figure 1). Only the tumor in patient 4 was dark brown. The surface of the tumor was typically smooth in all cases (Figure 1, C), and in 10 patients it was multinodular but still smooth (Figure 1, B and E). The meridional location of the tumor on the iris was inferotemporal in 7 patients, inferonasal in 4 patients, supertemporal in 4 patients, nasal in 2 patients, superior in 1 patient, inferior in 1 patient, and temporal in 1 patient (Table). The epicenter of the tumor was located in the peripheral iris in 16 patients, the midzone of the iris in 2, and near the pupillary margin in 2. Sizes ranged from to 2 × 2 × 1 to 7 × 7 × 4 mm.

In 17 patients, the tumor was visible in the anterior chamber with slitlamp biomicroscopy and gonioscopy and appeared to extend through the peripheral iris from the posterior pigment epithelium (Figure 1, A, B, C, and E). In 1 patient, the tumor was not visualized in the anterior chamber but had produced anterior displacement and slight thinning of the iris stroma, and the tumor was visualized clearly after the pupil was dilated (Figure 1, G). In 2 patients, the lesion appeared at the pupillary margin and extended slightly into the pupil. In no patient did the lesion appear to arise from the iris stroma. The adenoma of the IPE characteristically caused thinning or disappearance of the overlying iris stroma, but the border of the tumor was sharply demarcated from the iris stroma (Figure 1, A, B, C, and E).

In only 4 of the 20 patients were there ocular abnormalities believed to be secondary to the tumor. These included slight subluxation of the lens (patient 4) and pigment dispersion from the tumor into the adjacent anterior chamber angle (patients 1, 14, and 16), 1 of which caused ipsilateral elevation of intraocular pressure (patient 1). With transcleral transillumination, 17 of the tumors cast an absolute shadow, 3 cast a relative shadow, and none showed evidence of ciliary body involvement. Ultrasonic biomicroscopy (UBM) was performed in 2 of the patients who were seen more recently. In both UBM showed a solid mass (Figure 1, D). One or more small cystic cavities were seen in both with UBM.

Management included local resection using iridocyclectomy in 2 of the larger tumors and observation in 18 patients. In only 1 patient (patient 1) did we document slight tumor enlargement. That tumor was observed for 10 years elsewhere and by us for 3 years before slight enlargement and elevated intraocular pressure prompted us to remove it using iridocyclectomy.11 The elevated intraocular pressure resolved after tumor removal and has remained normal for more than 17 years. In the other patient (patient 4), the tumor was apparently growing, because of its larger size and symptomatic subluxation of the lens. In that instance, tumor resection was performed without a period of observation.14 In another instance (patient 18), the patient's family stated that the tumor had grown, but treatment was not recommended because the tumor was located in the patient's only useful eye. In that instance, the IPE adenoma appeared to be stable with 1-year observation only (Figure 1, C). No convincing tumor enlargement has been documented in any of the 18 patients observed without treatment during periods ranging from 6 months to 9 years (mean, 5 years).

Histopathologic examination of the 2 tumors that were managed by surgical resection revealed a deeply pigmented mass that arose from the IPE. In each case, the tumor was composed largely of irregular cords and acini of bland pigment epithelial cells that were separated by septae of fibrous connective tissue (Figure 1, F and H). The tumor cells contained large, round melanin granules. The tumor in patient 1 had cystic spaces that contained free-floating, deeply pigmented melanophages (Figure 1, F). These cystic spaces seemed to correlate with the multinodular surface characteristics of the tumor.

COMMENT

Most reported series of iris tumors have included little or no mention of adenoma of the IPE. In 1958, Duke and Dunn19 reported a series of 43 histopathologically documented iris tumors from the Wilmer Ophthalmological Institute and identified no cases of tumors of the IPE. In 1965, Ferry20 reported a series of 24 eyes enucleated with the erroneous diagnosis of iris melanoma, none of which were due to tumors of the IPE. In a series of 200 consecutive patients with lesions simulating iris melanoma,
only 1 patient (patient 1 of this series) with adenoma of the IPE was identified.\(^\text{21}\)

In 1964, Ashton\(^\text{7}\) reported a series of 145 iris tumors submitted to the Department of Pathology at the Institute of Ophthalmology in London, England, and identified only 2 cases of adenoma of the IPE, which he called benign melanomata of the IPE. Both patients were treated using iridectomy, and both remained alive and well after 5 and 11 years. In 1968, Morris and Henkind\(^\text{8}\) reported 2 cases of adenoma of the IPE, which he called adenoma of the IPE. In 1996, Spraul et al\(^\text{18}\) reported a single case and cited only 2 previously reported acceptable cases of adenoma of the IPE in the world literature.

Except for 1 case that was diagnosed and observed without treatment, 17 reports of adenoma of the IPE have been single-case descriptions in which the tumor was removed surgically. Our series of 20 patients, including 18 tumors that were diagnosed clinically and observed without treatment, is unique. It provides information about the clinical features and clinical course of adenoma of the IPE that has not been previously available.

Adenoma of the IPE usually is diagnosed in adulthood. In our series, the mean age at diagnosis was 60 years; in the literature review by Spraul et al,\(^\text{18}\) it was 47 years. The tumor appeared at 11 years of age in 1 of our patients (patient 1), and the tumor in the patient described by Rennie et al\(^\text{16}\) was first recognized at 5 years of age. Based on our observations, we cannot exclude the possibility that some adenomas of the IPE may be congenital but are not recognized until later in life, when they erode through the overlying iris stroma and become clinically evident. In 2 iridociliary cases reported in young children, there were other congenital abnormalities in the affected eye, suggesting that the tumor may have been present at birth.\(^\text{22,23}\)

Adenoma of the IPE does not appear to have a predisposition for sex, with 10 male and 10 female patients in our series. Of our 20 patients, 17 patients were white, 2 patients were African American, and 1 patient was Hispanic. Although the patient's race is not always mentioned in reported cases, we are not aware of any predisposition for race, such as that which occurs with uveal melanoma. Adenoma of the IPE usually does not cause visual impairment, with most of our patients being asymptomatic, except for 1 patient with slight subluxation of the lens.

Clinically, adenoma of the IPE is generally a small tumor, ranging from 1 to 7 mm in diameter. The 20 tumors in our series were dark gray to black, with the exception of the tumor in patient 4, which was dark brown. The tumor reported by Lowe and Greer\(^\text{9}\) was cream colored, and the tumor reported by Rennie et al\(^\text{16}\) was variably pigmented. In most instances, adenoma of the IPE is a solitary lesion, but the unusual case reported by Tso et al\(^\text{13}\) appeared to have multiple lesions arising from the IPE.

A characteristic feature of an adenoma of the IPE is anterior displacement and thinning of the iris stroma, which eventually erodes, disclosing the tumor on slit-lamp biomicroscopy. In some cases, the tumor can extend across the anterior chamber to touch the posterior surface of the cornea.\(^\text{8}\) In none of our patients, however, did the tumor appear to actively involve the iris stroma, as occurs with iris nevus, melanocytoma, and melanoma. Despite apparent slow progression, growth of the tumor is rarely recognized.

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**Clinical Data on 20 Patients With Adenoma of the Iris Pigment Epithelium**

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y/Race</th>
<th>Year</th>
<th>Eye</th>
<th>Visual Acuity†</th>
<th>Iris Zone</th>
<th>Iris Meridian</th>
<th>Tumor Size, mm</th>
<th>Eye Findings</th>
<th>Management</th>
<th>Last Follow-up (Length of Follow-up, y)</th>
</tr>
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<tbody>
<tr>
<td>1/M/11/W 1977 L 6/6 Peripheral IT 7×7×4</td>
<td>1977</td>
<td>L</td>
<td>6/6</td>
<td>Peripheral IT</td>
<td>7×7×4</td>
<td>Glaucoma, angle seeds</td>
<td>Resection after 4 y</td>
<td>Stable after surgery (17)</td>
<td></td>
</tr>
<tr>
<td>2/M/84/W 1979 L 6/7.5 Peripheral IN 2×2×2</td>
<td>1979</td>
<td>L</td>
<td>6/7.5</td>
<td>Peripheral IN</td>
<td>2×2×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (2)</td>
<td></td>
</tr>
<tr>
<td>4/M/32/AA 1984 R 6/12 Midzone IN 5×5×5</td>
<td>1984</td>
<td>R</td>
<td>6/12</td>
<td>Midzone IN</td>
<td>5×5×5</td>
<td>Subluxed lens</td>
<td>Resection</td>
<td>Stable after surgery (14)</td>
<td></td>
</tr>
<tr>
<td>5/I/76/AA 1985 R 6/6 Peripheral IT 2×2×2</td>
<td>1985</td>
<td>R</td>
<td>6/6</td>
<td>Peripheral IT</td>
<td>2×2×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (1)</td>
<td></td>
</tr>
<tr>
<td>6/I/67/W 1989 L 6/6 Peripheral IN 2×2×2</td>
<td>1989</td>
<td>L</td>
<td>6/6</td>
<td>Peripheral IN</td>
<td>2×2×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (6)</td>
<td></td>
</tr>
<tr>
<td>7/I/32/W 1989 R 6/7.5 Peripheral IT 3×3×2</td>
<td>1989</td>
<td>R</td>
<td>6/7.5</td>
<td>Peripheral IT</td>
<td>3×3×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (9)</td>
<td></td>
</tr>
<tr>
<td>8/I/47/W 1990 L 6/6 Peripheral ST 2×2×1</td>
<td>1990</td>
<td>L</td>
<td>6/6</td>
<td>Peripheral ST</td>
<td>2×2×1</td>
<td>None</td>
<td>Observation</td>
<td>Stable (8)</td>
<td></td>
</tr>
<tr>
<td>9/I/78/W 1990 R 6/18 Peripheral S 2×2×1</td>
<td>1990</td>
<td>R</td>
<td>6/18</td>
<td>Peripheral S</td>
<td>2×2×1</td>
<td>Cataract††</td>
<td>Observation</td>
<td>Stable (8)</td>
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<tr>
<td>10/I/58/W 1991 L 6/9 Peripheral IN 2×2×2</td>
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<td>L</td>
<td>6/9</td>
<td>Peripheral IN</td>
<td>2×2×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (7)</td>
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<tr>
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<td>1992</td>
<td>L</td>
<td>6/7.5</td>
<td>Pupil IT</td>
<td>3×3×2</td>
<td>Iris seeds</td>
<td>Observation</td>
<td>Stable (6)</td>
<td></td>
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<tr>
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<td>L</td>
<td>6/6</td>
<td>Peripheral ST</td>
<td>4×4×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (2)</td>
<td></td>
</tr>
<tr>
<td>13/M/65/W 1994 R 6/6 Peripheral ST 2×2×1</td>
<td>1994</td>
<td>R</td>
<td>6/6</td>
<td>Peripheral ST</td>
<td>2×2×1</td>
<td>Iris seeds</td>
<td>Observation</td>
<td>Stable (3)</td>
<td></td>
</tr>
<tr>
<td>14/M/77/W 1995 L 6/6 Peripheral IT 4×4×2</td>
<td>1995</td>
<td>L</td>
<td>6/6</td>
<td>Peripheral IT</td>
<td>4×4×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (3)</td>
<td></td>
</tr>
<tr>
<td>16/I/63/W 1996 L 6/6 Peripheral I 4×4×2</td>
<td>1996</td>
<td>L</td>
<td>6/6</td>
<td>Peripheral I</td>
<td>4×4×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (2)</td>
<td></td>
</tr>
<tr>
<td>17/M/47/H 1996 L 6/6 Midzone IT 2×2×1</td>
<td>1996</td>
<td>L</td>
<td>6/6</td>
<td>Midzone IT</td>
<td>2×2×1</td>
<td>None</td>
<td>Observation</td>
<td>Stable (1)</td>
<td></td>
</tr>
<tr>
<td>18/I/74/W 1997 R 6/6 Peripheral N 4×4×3</td>
<td>1997</td>
<td>R</td>
<td>6/6</td>
<td>Peripheral N</td>
<td>4×4×3</td>
<td>None</td>
<td>Observation</td>
<td>Stable (1)</td>
<td></td>
</tr>
<tr>
<td>19/F/85/W 1997 L Finger counting Peripheral N 2×2×1</td>
<td>1997</td>
<td>L</td>
<td>Finger counting</td>
<td>Peripheral N</td>
<td>2×2×1</td>
<td>ARMD‡</td>
<td>Observation</td>
<td>Stable (1)</td>
<td></td>
</tr>
<tr>
<td>20/M/55/W 1998 R 6/6 Peripheral IT 2×2×2</td>
<td>1998</td>
<td>R</td>
<td>6/6</td>
<td>Peripheral IT</td>
<td>2×2×2</td>
<td>None</td>
<td>Observation</td>
<td>Stable (&lt;1)</td>
<td></td>
</tr>
</tbody>
</table>

*W indicates white; AA, African American; H, Hispanic; L, left; R, right; I, inferior; S, superior; N, nasal; T, temporal; and ARMD, age-related macular degeneration.
†In meters.
‡Indicates findings not directly related to the adenoma of the iris pigment epithelium.

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Histopathologically, reported cases of adenoma of the IPE have had rather consistent features. Results of low-magnification microscopy show a deeply pigmented tumor that appears to arise from adjacent normal IPE. It tends to compress the iris stroma, but not infiltrate the stroma. It is characterized cytologically by irregular cords and tubules of well-differentiated pigment epithelial cells, separated by connective tissue septae. Cystoid spaces that contain melanophages occasionally are found within the tumor. In rare instances, tumors of the IPE have been classified as malignant (adenocarcinoma) based on local invasiveness and cellular pleomorphism.

We suspect that adenoma of the IPE is more common than one would predict from the paucity of reported cases. It is likely that some adenomas of the IPE lie hidden behind the iris stroma and are not detected clinically. It is also possible that some tumors that erode through the iris stroma are diagnosed as benign nevi and are observed without an opinion from an experienced ocular oncologist. Only the larger or more suspicious tumors that are resected and documented histopathologically are likely to be reported.

There are several conditions that should be included in the differential diagnosis of adenoma of the IPE (Figure 2). Perhaps the most important aspect of adenoma of the IPE lies in its differentiation from iris and ciliary body melanoma and nevus, particularly the melanocytoma variant of nevus. Adenoma of the IPE arises from the posterior pigment epithelial layer of the iris, and it tends to displace the iris stroma. In contrast, iris nevi and melanomas arise from the iris stroma and blend with the stroma. (Figure 2, A and B). Tumors of the IPE usually are dark gray to black, whereas most melanomas are brown, relatively less pigmented, and often flesh-colored or amelanotic. Adenoma of the IPE rarely displays prominent blood vessels, whereas melanoma is more likely to have feeder vessels and tumor vascularity. Adenoma of the IPE usually has abruptly elevated margins, whereas iris melanoma often has more tapering margins that are clearly located within the iris stroma.

![Figure 1. Clinical, ultrasonographic, and pathological features of adenomas of the iris pigment epithelium (IPE). A, Subtle adenoma of IPE in the peripheral iris inferonasally in the left eye of patient 16. B, Gonioscopic view of the lesion shown in part A. Smooth surface to the bilobed lesion, which does not affect the iris stroma, is seen. C, Larger adenoma of the IPE located temporally in the right eye of patient 18. D, Ultrasonic biomicroscopy of adenoma of the IPE in patient 17. The lesion is posterior to the peripheral aspect of the iris and has acoustic solidity. E, Irregular multinodular adenoma of the IPE located inferotemporally in patient 1. F, Histopathologic findings of the lesion shown in part E after iridocyclectomy. The cords and acini of pigment epithelial cells are seen. The cystoid spaces, containing melanophages, probably accounted for the multinodular appearance of the lesion (hematoxylin-eosin, original magnification x20). G, Large adenoma of the IPE situated behind the iris and seen through the dilated pupil in patient 4. This lesion has a smooth surface. It is causing anterior displacement of the iris but has not appeared in the anterior chamber. H, Histopathologic findings of the lesion shown in part G after iridocyclectomy. The cords and acini of pigment epithelial cells that comprise the tumor are seen (hematoxylin-eosin, original magnification x20).](image-url)
Adenoma of the IPE should also be differentiated from ciliary body melanoma. Both tumors can cause anterior displacement of the peripheral portion of the iris. However, results of careful slitlamp biomicroscopy, gonioscopy, and transillumination suggest that adenoma of the IPE is a tumor that arises from the iris and not the ciliary body. Accurate transillumination of an adenoma of the IPE usually does not reveal a shadow in the pars plana region, whereas most ciliary body melanomas cast a shadow that involves the pars plicata and the pars plana. Adenoma of the IPE does not tend to produce dilated episcleral blood vessels, whereas sentinel vessels are common overlying ciliary body melanoma.

Another tumor that can resemble an adenoma of the IPE is an iris melanocytoma. This is a variant of nevus that rarely can give rise to malignant melanoma. Like adenoma of the IPE, it is also a deeply pigmented solid mass. However, it clearly involves the iris stroma, is dark brown rather than gray black, usually has a rough or corrugated surface rather than a smooth surface (Figure 2, C and D), and is more likely to become necrotic and induce pigment dispersion and secondary glaucoma.

Adenoma of the IPE should also be differentiated from cyst of the IPE, especially midzonal and peripheral cysts. The classification and diagnostic approaches to IPE cysts have been published in comprehensive reports. The midzonal cyst of the IPE has a smooth, velvety surface, and it tends to become more fusiform in shape with dilation of the pupil (Figure 2, E). With UBM, the midzonal cyst appears as an echolucent lesion behind the midportion of the iris (Figure 2, F). The more peripheral or iridociliary cyst can produce anterior displacement of the iris stroma, similar to adenoma of the IPE. However, results of gonioscopy with the pupil widely dilated show a clear, transparent cyst (Figure 2, G) rather than a solid pigmented mass. Results of UBM of a peripheral cyst show a round echolucent lesion in the iridociliary sulcus, posterior to the peripheral aspect of the iris (Figure 2, H). A free-floating cyst can migrate into the anterior chamber, become fixed in the angle, and can closely resemble an adenoma of the IPE. However, the cyst lies entirely anterior to the iris stroma, and it locally transmits light. In some cases of IPE adenoma, small echolucent cysts are seen within the solid mass, prob-
ably corresponding to the cystoid spaces that were seen histopathologically in our first patient. Ultrasonic biomicroscopy is advisable in instances where the differential diagnosis is uncertain.

We are reporting our experience with the clinical and histopathologic features of adenomas of the ciliary body pigment epithelium and retinal pigment epithelium. These more posteriorly located tumors of the pigmented neuroepithelium are frequently more aggressive clinically and have different histopathologic features than the tumors of the IPE described herein.

Adenoma of the IPE is a distinct intraocular tumor that has rather characteristic clinical features and a benign clinical course. Although it was previously believed to be difficult or impossible to differentiate from iris melanoma or iris nevus, our observations indicate that it has typical features that should suggest the correct diagnosis. This benign tumor should be observed periodically, and local tumor resection should be considered if there is progressive growth, secondary glaucoma, or subluxation of the lens.

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